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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,506	09/19/2000	Paolo Cozzi	P101615-0007	9195

7590

06/10/2002

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 06/10/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/623,506

Applicant(s)

COZZI ET AL.

Examiner

Jeffrey E. Russel

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1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2002 and 30 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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1. Formula (I) in the clean copy of amended claim 1 contained in the response filed April 26, 2002 differs from Formula (I) in the marked-up copy of amended claim 1 in that the former is missing a bond sign which should be present in the acryloyl group. Any future amendments should be carefully checked to ensure accurate reporting of all amendments to the claims.

2. Claims 1-4 and 6-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1, Formula (I), and claim 6, part (b), Formula (IV), the bond sign which should be present in the acryloyl group is missing. Claim 1, proviso (b), is confusing because it refers to "the heterocyclic rings within the polyheterocyclic chain".

However, the structure of formula (I) is never directly described as a polyheterocyclic chain, and the only rings within the chain are now pyrazole rings, not heterocyclic rings in general. Further, the proviso requires at least one of the heterocyclic rings to be other than pyrrole, whereas Formula (I) already requires the heterocyclic rings to be pyrazole. It is accordingly unclear whether proviso (b) is automatically satisfied by Formula (I) as amended, or whether proviso (b) permits any of the pyrazole rings in Formula (I) to be substituted by any heterocyclic ring as long as not all of the pyrazole rings are substituted by pyrrole rings.

3. Claim 5 is objected to because of the following informalities: At claim 5, page 9 of the amendment filed April 30, 2002, line 11, "carboxamido" (first occurrence) is misspelled.

Appropriate correction is required.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/04524 in view of the WO Patent Application 96/05196. The WO Patent Application '524 teaches acryloyl-substituted distamycin derivatives useful as antitumor agents which differ from Applicants' claimed compounds in that the compounds of the WO Patent Application '524 contain only pyrrole as the heterocyclic ring, whereas Applicants' claims require at least one of the heterocyclic rings to be other than pyrrole. The WO Patent Application '196 teaches the substitution of pyrrole rings in a distamycin A analog either partially or completely with other heteromonocyclic rings, especially with imidazole or pyrazole rings (see, e.g., the Abstract; page 1, lines 12-14; page 5, lines 17-18; and pages 7-18). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to substitute imidazole or pyrazole rings for some or all of the pyrrole rings of the compounds of the WO Patent Application '524 because the WO Patent Application '196 teaches such substitutions in analogous distamycin compounds and because the resulting compounds have only the expected antitumor activity.

6. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/04524 in view of the WO Patent Application 96/05196 as applied against claims 1-11 above, and further in view of the Baraldi et al article. As noted above, the WO Patent Application '524 does not teach a compound in which at least one of the heterocyclic rings is other than pyrrole. The Baraldi et al article teaches distamycin derivatives 12 and 13 comprising an initial imidazole or pyrazole ring which has improved in vivo antitumor activity in comparison with distamycin derivative 3 which has an initial pyrrole ring. See, e.g., page 1241; Scheme 1; and page 1244, Table 1. Accordingly, it would have been obvious to one of ordinary

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skill in the art at the time Applicants' invention was made to substitute an imidazole or pyrazole ring for the initial pyrrole ring in the distamycin derivatives of the WO Patent Application '524 because the WO Patent Application '196 teaches such ring substitutions in analogous distamycin compounds and because the Baraldi et al suggests that such a substitution would have been expected to increase the in vivo antitumor activity of a distamycin derivative.

7. Applicant's arguments filed April 26, 2002 and April 30, 2002 have been fully considered but they are not persuasive.

Applicants discuss the amendments they have made to the claims at page 19, second full paragraph, of the response filed April 26, 2002. However, the structure set forth in the remarks is not the same as the structure set forth in the claims. Further, as claim 1, proviso (b), indicates that any heterocyclic ring within the polyheterocyclic chain can be other than pyrrole, the acryloyl moiety does not first have to be connected to a pyrazole ring.

The WO Patent Application 98/04524 is relevant prior art because it discloses acryloyl-substituted distamycin derivatives useful as antitumor agents, the same types of compounds used for the same purpose as Applicants' claimed compounds. While the WO Patent Application '524 by itself may not anticipate or suggest Applicants' claims, this does not mean that the reference is not relevant. Further, the fact that the WO Patent Application '524 by itself may not anticipate or suggest Applicants' claims is irrelevant to the rejections of record, which are based upon combinations of references under 35 U.S.C. 103. The combination of references under 35 U.S.C. 103 in order to suggest Applicants' claims is permitted by the statute and the case law.

Applicants argue that their compounds exhibit an unexpected increase in activity compared to the compounds of the Baraldi et al article. Firstly, the attached table can not be

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relied upon to establish unexpected results because it was not submitted in appropriate form under 37 CFR 1.132. Secondly, the results reported in the attached table are not commensurate in scope with the rejected claims because the table does not report tests of compounds representative of the full range of structures encompassed by instant claim 1. In particular, compounds representative of all of the B groups specified in claim 1 are not tested, and compounds representative of the full range of heterocyclic rings permitted in Formula (I) are not tested (although see the above rejection under 35 U.S.C. 112, second paragraph, with respect to claim 1, proviso (b)).

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

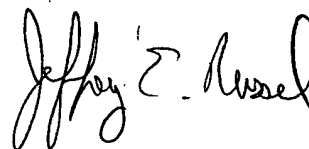
Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

A handwritten signature in black ink, appearing to read "Jeffrey E. Russel". The signature is fluid and cursive, with the first name "Jeffrey" being more prominent and the last name "Russel" following it.

Jeffrey E. Russel

Primary Patent Examiner

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JRussel

June 6, 2002